REMARKS

Claims 28-41, 55 and 56 are pending. Claim 54 is canceled. Claims 28-37, 39-41, 55 and 56 are amended. The amendments find basis in the application as originally filed. No new matter is added.

Applicant notes that an Information Disclosure Statement, along with Form PTO-1449 and cited references are enclosed herewith for filing in connection with this application.

THE REJECTION OF CLAIMS 31, 36-38, 39-41 and 54-56 UNDER 35 U.S.C. §112, SECOND PARAGRAPH

The Office Action alleges that claims 31, 36-38, 39-41 and 54-56 are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Recitation of the term "analogs and derivatives"

The Office Action alleges that the recitation of analogs and derivatives in claims 31, 36-38 and 56 render the claims indefinite.

Applicant respectfully submits that pending claim 38 does not recite the term "analogs and derivatives."

As amended herein, claims 31, 36-37 and 56 do not recite the term "analogs and derivative". The claims recite "pharmaceutically acceptable salts". The specification defines pharmaceutically acceptable salts as follows:

> Pharmaceutically acceptable salt means salts that are pharmaceutically acceptable and have the desired pharmacological properties. Such salts include salts that may be formed where acidic protons present in the compounds are capable of reacting with inorganic or organic bases. Suitable inorganic salts include those formed with the alkali metals, e.g. sodium and potassium, magnesium, calcium, and aluminum. Suitable organic salts include those formed with organic bases such as the amine bases, e.g. ethanolamine, diethanolamine, triethanolamine, tromethamine, N-methylglucamine, and the like. Such salts also include acid addition salts formed with inorganic acids (e.g. hydrochloric and hydrobromic acids) and organic acids (e.g. acetic acid, citric acid, maleic acid, and the alkane- and arene-sulfonic acids such as methanesulfonic acid and benzenesulfonic acid). When there are two acidic groups present, a pharmaceutically acceptable salt may be a

> mono-acid-mono-salt or a di-salt; and similarly where there are more than two acidic groups present, some or all of such groups can be salified.

Therefore the term is clearly defined in the specification and claims are not indefinite for the recitation of pharmaceutically acceptable salts.

Recitation of the term "substantially"

Claims 39-41 and 55 are rejected as being indefinite for recitation of the term "substantially." The Office Action alleges that the term "substantially" is not defined in the claim and specification does not provide a standard for ascertaining the requisite degree. The Office Action urges that one of ordinary skill in the art would not be reasonably apprised of the scope of the claimed subject matter.

Applicant respectfully submits that pending claim 39 does not recite the term "substantially."

Amended claims 40-41 and 55 recite that the compounds are at least 70% pure. Basis for this amendment is found in the specification on page 40, line 24-28, which recite:

> As defined herein, a substantially pure compound or combination of compounds is at least about 70% pure, more advantageously at least 80-% pure, at least 90% pure, more preferably greater than 90% pure, e.g., at least 90-95% pure, or even purer such as greater than 95% pure, e.g., 99.99% pure.

Reconsideration and removal of the objection is requested.

Recitation of the term "or the like"

Claim 54 is rejected as being indefinite for recitation of the term "or the like." Claim 54 is canceled herein, thereby rendering the objection moot.

THE REJECTION OF CLAIMS 28-41 and 54-56 UNDER 35 U.S.C. §102(b), OVER KUZNICKI *ET AL.*

Claims 28-41 and 54-56 are rejected under 35 U.S.C. § 102(b) as being anticipated by Kuznicki *et al.* (U.S. Patent No. 5,681,569) because the cited reference allegedly discloses a composition containing green tea solids extracted from tea material. The extract contains 0.01-0.35% flavanols and catechins, wherein the catechin or a mixture of two or more catechins are catechin, epicatechin, gallocatechin, epigallocatechin gallate and epicatechin gallate, and a

pharmaceutical carrier. The Office Action alleges that the green tea composition of Kuznicki *et al.* inherently comprises proanthocyanidins oligomers having the instant formula I and II and/or procyanidins such as the dimers and trimers of catechin and epicatechin because catechins are allegedly known to encompass these compounds which are known to be isolated from green tea. The Office Action further urges that the therapeutically effective amount of a catechin or mixture of catechins claimed in instant claims is disclosed in examples I and III.

This rejection is respectfully traversed.

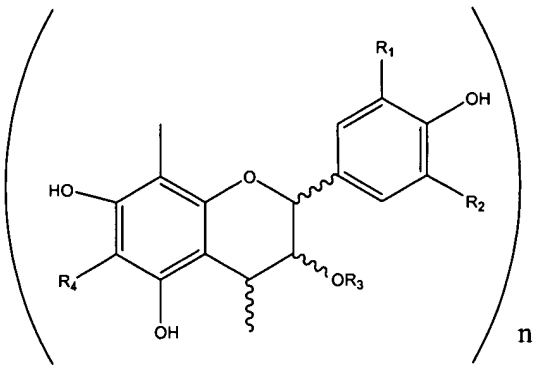
RELEVANT LAW

Anticipation requires the disclosure in a single prior art reference of each element of the claim under consideration. *In re Spada*, 15 USPQ2d 1655 (Fed. Cir, 1990), *In re Bond*, 15 USPQ 1566 (Fed. Cir. 1990), *Soundscriber Corp. v. U.S.*, 360 F.2d 954, 148 USPQ 298, 301, adopted 149 USPQ 640 (Ct. Cl.) 1966. See, also, *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913,1920 (Fed. Cir.), *cert. denied*, 110 S.Ct. 154 (1989). "[A]ll limitations in the claims must be found in the reference, since the claims measure the invention". *In re Lang*, 644 F.2d 856, 862, 209 USPQ 288, 293 (CCPA 1981). Moreover it is incumbent on the Examiner to identify wherein each and every facet of the claimed invention is disclosed in the reference. *Lindemann Maschinen-fabrik Gmbh v. American Hoist and Derrick Co.*, 730 F.2d 1452, 221 USPQ 481 (Fed. Cir. 1984). Further, the reference must describe the invention as claimed sufficiently to have placed a person of ordinary skill in the art in possession of the invention. An inherent property has to flow naturally from what is taught in a reference *In re Oelrich*, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981).

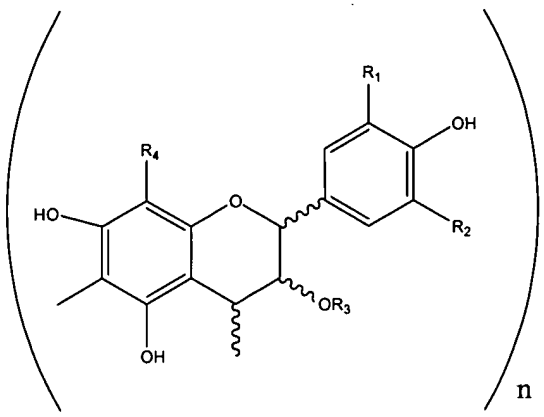
THE CLAIMS

Applicant notes that rejection to claims 54 is rendered moot by cancelation thereof. Amended claim 28 is directed to a pharmaceutical composition containing therapeutically effective amount of a proanthocyanidin, selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations of Formula I and Formula II, and pharmaceutically acceptable salts of the foregoing proanthocyanidins and a pharmaceutically acceptable carrier, diluent, or excipient, the

therapeutic amount of the proanthocyanidin selected for efficacy in treating amyloid, α - synuclein or NAC fibrillogenesis in a mammalian subject. The claims describe formula I and II as follows:



Formula I



Formula II

Claims 29-41 depend from claim 28 and further define the therapeutically effective amount and the proanthocyanidins of claim 28.

Claim 55 is an independent claim directed to a pharmaceutical composition containing a therapeutically effective amount of a mixture of at least 70% pure proanthocyanidins selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations thereof, and pharmaceutically acceptable salts of the foregoing proanthocyanidins.

Claim 56 depends from claim 55 and further defines the proanthocyanidins of claim 55.

Disclosure of Kuznicki *et al.*

Kuznicki *et al.* discloses a liquid composition containing flavanols, sodium and potassium ions, carbohydrate and water. The reference also discloses a dry composition containing flavanols, sodium and potassium ions, carbohydrate (column 2, lines 12-32). The reference further discloses that the term flavanol or catechin means primarily catechin, epicatechins, and their derivatives (column 3, lines 20-21). It is further described in the reference that the flavanols used therein can be extracted from fruit, vegetables, green tea or other natural sources (column 4, lines 9-11).

Differences between the claimed subject matter and the disclosure of Kuznicki *et al.*

Claims 28-41

Kuznicki *et al.* does not disclose a pharmaceutical composition containing therapeutically effective amount of a proanthocyanidin, selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations of Formula I and Formula II, where n is 2-20, and pharmaceutically acceptable salts of the foregoing proanthocyanidins and a pharmaceutically acceptable carrier, diluent, or excipient. The reference describes the compositions as containing flavanols and further discloses that the term flavanol or catechin means primarily catechin, epicatechins, and their derivatives. The reference does not disclose that the compositions described therein contain oligomers of catechins or epicatechins, where the oligomers contain 2-20 monomers of catechins or epicatechins or combinations of monomers of catechins or epicatechins. The compositions in the reference contain catechins or mixtures of two or more catechins.

Further, the compositions claimed in the instant claims contain therapeutically effective amount of a proanthocyanidin, selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations thereof, and pharmaceutically acceptable salts of the foregoing proanthocyanidins selected for efficacy in treating amyloid in a mammalian subject. Since the cited reference does not disclose proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations of Formula I and Formula II, and pharmaceutically acceptable salts of the foregoing proanthocyanidins, it can not disclose compositions containing therapeutic amount thereof effective for treating amyloid in mammalian subjects.

Thus, the cited reference does not disclose, either literally or inherently, every element of the claimed composition. Therefore, Kuznicki *et al.* does not anticipate a composition containing a proanthocyanidin as claimed in claim 28. Because claims 29-41 depend from claim 28, Kuznicki *et al.* does not anticipate any of the claims dependent on claim 28. Applicant respectfully requests that the rejection be reconsidered and withdrawn.

Claim 55-56

Kuznicki *et al.* does not disclose a mixture of at least 70% pure proanthocyanidins selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations thereof, and pharmaceutically acceptable salts of the foregoing proanthocyanidins. As discussed above, the reference describes compositions containing flavanols and further discloses that the term flavanol or catechin means primarily catechin, epicatechins, and their derivatives. The reference can not disclose a composition containing a therapeutically effective amount of a mixture of at least 70% pure proanthocyanidins selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations of Formula I and Formula II because it does not disclose the proanthocyanidins of formula I and II. Therefore, the reference does not disclose the composition of claim 55.

Thus, the cited reference does not disclose, either literally or inherently, every element of the claimed compositon. Therefore, Kuznicki *et al.* does not anticipate a composition containing therapeutically effective amount of a mixture of at least 70% pure proanthocyanidins as claimed in claim 55. Because claim 56 depends from claim 55, Kuznicki *et al.* does not anticipate claim 56. Applicant respectfully requests that the rejection be reconsidered and withdrawn.

Rebuttal to Examiner's Arguments

The Office Action alleges that the green tea composition of Kuznicki et al. inherently comprises proanthocyanidins oligomers having formula I and II herein and/or procyanidins such as the dimers and trimers of catechin and epicatechin herein because catechins are allegedly known to encompass these compounds which are known to be isolated from green tea.

Applicant respectfully submits that the cited reference discloses green tea extracts that contain catechins. The reference does not disclose proanthocyanidins selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations thereof, and pharmaceutically acceptable salts of the foregoing proanthocyanidins. The Examiner has not provided any further reference to support the allegation that green extract contains proanthocyanidins oligomers as claimed herein.

Therefore, the allegation that the green tea composition of Kuznicki *et al.* inherently comprises proanthocyanidin oligomers having formula I and II herein and/or procyanidins such as the dimers and trimers of catechin and epicatechin is without any support. Applicant respectfully submits that if Examiner is aware of any such art, it be made of record.

THE REJECTION OF CLAIMS 28, 31-41 and 54-56 UNDER 35 U.S.C. §102(b)

Claims 28, 31-41 and 54-56 are rejected under 35 U.S.C. § 102(b) as being anticipated by JP 10245342 because the reference allegedly discloses a pharmaceutical composition for diminishing the toxicity in nerve cells caused by β-amyloid protein containing a catechin or two or more of catechin such as epigallocatechin gallate and epicatechin gallate prescribed in effective amounts for diminishing the toxicity of β-amyloid protein, and a pharmaceutical carrier. The Office Action alleges that the green tea composition disclosed in the cited reference inherently contains proanthocyanidins oligomers having formula I and II and/or procyanidins such as the dimers and trimers of catechin and epicatechin because catechins are allegedly known to encompass these compounds which are known to be isolated from green tea.

RELEVANT LAW

As discussed above.

Disclosure of JP 10245342

JP 10245342 discloses that green tea extract contains polyphenols such as tea catechin and/or theaflavin. The reference describes that the composition containing tea catechins and/or theaflavin can be used for diminishing the toxicity in nerve cells caused by β-amyloid protein. The reference does not disclose a composition containing a therapeutically effective amount of proanthocyanidins selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations of Formula I and Formula II, and pharmaceutically acceptable salts of the foregoing proanthocyanidins.

Differences between the claimed subject matter and the disclosure of JP 10245342

Claims 28 and 31-41

The compositions disclosed in JP 10245342 do not contain proanthocyanidins selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations of Formula I and Formula II, and pharmaceutically acceptable salts of the foregoing proanthocyanidins. The reference clearly describes that the compositions contain tea catechin and/or theaflavin. The instant claims are directed to compositions containing proanthocyanidins selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations thereof, and pharmaceutically acceptable salts of the foregoing proanthocyanidins. The reference does not disclose the compounds of formula I or II or the oligomeric combinations thereof. Therefore, it can not disclose a pharmaceutical composition containing a therapeutically effective amount of these compounds and a pharmaceutically acceptable carrier, diluent, or excipient. The compositions in the reference contain green tea extract that contains tea polyphenols including tea catechin and/or theaflavin. JP 10245342 does not describe compositions containing oligomers of epicatechis, catechins or oligomeric combinations of epicatechis and catechins.

Thus, the cited reference does not disclose, either literally or inherently, every element of the claimed compositon. Therefore, JP 10245342 does not anticipate a composition containing a proanthocyanidins selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations of Formula I and Formula II, and pharmaceutically acceptable salts of the foregoing proanthocyanidins, as claimed in claim 28. Because claims 31-41 depend from claim 28, JP 10245342 does not anticipate any of the claims dependent on claim 28. Applicant respectfully requests that the rejection be reconsidered and withdrawn.

Claim 55-56

As discussed above the reference does not disclose proanthocyanidins selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins

characterized by oligomeric combinations thereof, and pharmaceutically acceptable salts of the foregoing proanthocyanidins. Therefore, the reference can not disclose a mixture of at least 70% pure proanthocyanidin, nor can it disclose a composition containing a therapeutically effective amount of a mixture of at least 70% pure proanthocyanidins, as claimed in claim 55.

Thus, the cited reference does not disclose, either literally or inherently, every element of the claimed compositon. Therefore, JP 10245342 does not anticipate a composition containing therapeutically effective amount of a mixture of at least 70% pure proanthocyanidins selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations of Formula I and Formula II, and pharmaceutically acceptable salts of the foregoing proanthocyanidins as claimed in claim 55. Because claim 56 depends from claim 55, JP 10245342 does not anticipate claim 56. Applicant respectfully requests that the rejection be reconsidered and withdrawn.

THE REJECTION OF CLAIMS 28, 31-41 and 54-56 UNDER 35 U.S.C. § 102(b) OVER HASHIMOTO *ET AL.*

Claims 28, 31-41 and 54-56 are rejected under 35 U.S.C. § 102(b) as being anticipated by Hashimoto *et al.* because Hashimoto *et al.* allegedly discloses a composition containing or inherently containing a catechin or two or more of catechins such as epigallocatechin and dimers or proanthocyanodins oligomers having the formula I and II herein and/or procyanidins such as the dimers and trimers of catechin and epicatechin in effective amounts and a pharmaceutical carrier. The Office Action urges that the oolong tea composition in Hashimoto *et al.* inherently comprises the instant compounds because these compounds are known to be isolated from oolong tea. This rejection is respectfully traversed.

RELEVANT LAW

As discussed above.

Disclosure of Hashimoto *et al.*

Hashimoto *et al.* discloses oolong tea extract in 80% aqueous acetone. The reference discloses polyphenolic constituents in oolong tea extract including a flavan-3-ol, dimeric flavan-3-ols and proanthocyanidins. The reference describes identification of individual compounds

based on their chemical and spectroscopic evidence. The reference does not disclose an aqueous extract that contains therapeutically effective amount of proanthocyanidins.

Differences between the claimed subject matter and the disclosure of Hashimoto *et al.*

Claim 28 and 31-41

Hashimoto *et al.* describes that an oolong tea extract in 80% aqueous acetone contains polyphenolic constituents including proanthocyanidins. It does not describe a pharmaceutical composition containing a therapeutically effective amount of a proanthocyanidin selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations thereof, and pharmaceutically acceptable salts of the foregoing proanthocyanidins and a pharmaceutically acceptable carrier, diluent, or excipient, wherein the therapeutic amount is selected for efficacy in treating amyloid in a mammalian subject. The reference does not disclose the instantly claimed pharmaceutical compositions because it does not disclose compositions containing a therapeutically effective amount of proanthocyanidins. Nor does the reference disclose a pharmaceutically acceptable carrier, diluent, or excipient, as required in the instantly claimed composition. The oolong tea extract in 80% aqueous acetone containing proanthocyanidins is not within the scope of the instantly claimed pharmaceutical composition.

Thus, the cited reference does not disclose, either literally or inherently, every element of the claimed composition. Therefore, Hashimoto *et al.* does not anticipate a composition containing therapeutically effective amount of proanthocyanidin as claimed in claim 28. Because claims 31-41 depend from claim 28, Hashimoto *et al.* does not anticipate claims 31-41. Applicant respectfully requests that the rejection be reconsidered and withdrawn.

Claim 55-56

Hashimoto *et al.* does not disclose a pharmaceutical composition containing a therapeutically effective amount of a mixture of at least 70% pure proanthocyanidins selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations of Formula I and Formula II, and

pharmaceutically acceptable salts of the foregoing proanthocyanidins. As discussed above, the reference describes oolong tea extract containing proanthocyanidins in 80% aqueous acetone. The reference further describes isolation of various components in the 80% aqueous acetone extract of oolong tea. The reference does not disclose an aqueous extract that contains therapeutically effective amount of a mixture of at least 70% pure proanthocyanidins.

Thus, the cited reference does not disclose, either literally or inherently, every element of the claimed compositon. Therefore, Hashimoto *et al.* does not anticipate a composition containing therapeutically effective amount of a mixture of at least 70% pure proanthocyanidins as claimed in claim 55. Because claim 56 depends from claim 55, Hashimoto *et al.* does not anticipate claim 56. Applicant respectfully requests that the rejection be reconsidered and withdrawn.

THE REJECTION OF CLAIMS 28, 31-41 and 54-56 UNDER 35 U.S.C. §102(b), OVER HATANO *ET AL.*

Claims 28, 31-41 and 54-56 are rejected under 35 U.S.C. § 102(b) as being anticipated by Hatano *et al.* because Hatano *et al.* allegedly discloses a composition for anti-HIV containing or inherently containing a catechin or two or more of catechins such as epigallocatechin and dimers of proanthocyanodins oligomers having the formula I and II herein and/or procyanidins such as the dimers and trimers of catechin and epicatechin in effective amounts and a pharmaceutical carrier. The Office Action urges that the compositions in the cited reference inherently contains the instant compounds because these compounds are known to be isolated from Camellia japonica plants. This rejection is respectfully traversed.

RELEVANT LAW

As discussed above.

Disclosure of Hatano *et al.*

Hatano *et al.* discloses eight tannins isolated from the leaf of Camellia japonica. The reference further discloses that the tannins isolated include complex tannins consisting of monomeric hydrolysable tannin and epicatechin, dimeric hydrolysable tannins and complex tannins composed of a dimeric hydrolysable tannin and epicatechin. The reference further discloses that the tannins isolated showed anti-HIV activity.

Differences between the claims and the disclosure of Hatano *et al.*

Claims 28 and 31-41

Hatano *et al.* does not describe a pharmaceutical composition containing a therapeutically effective amount of a proanthocyanidin selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations thereof, and pharmaceutically acceptable salts of the foregoing proanthocyanidins, wherein the therapeutic amount is selected for efficacy in treating amyloid in a mammalian subject. Hatano *et al.* discloses that an extract from leaf of Camellia japonica contains complex tannins consisting of monomeric hydrolysable tannin and epicatechin, dimeric hydrolysable tannins and complex tannins composed of a dimeric hydrolysable tannin and epicatechin. The reference does not disclose that the extract contains proanthocyanidins of Formula I or Formula II, and oligomeric combinations thereof.

Further, the compositions claimed in the instant claims contain therapeutic amount of the proanthocyanidins selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations of Formula I and Formula II, and pharmaceutically acceptable salts of the foregoing proanthocyanidins, selected for efficacy in treating amyloid in a mammalian subject. Since the cited reference does not disclose proanthocyanidins of formula I or II and the oligomeric combinations thereof, it can not disclose compositions containing therapeutic amount thereof effective for treating amyloid in mammalian subjects.

Thus, the cited reference does not disclose, either literally or inherently, every element of the claimed composition. Therefore, Hatano *et al.* does not anticipate a composition containing therapeutically effective amount of proanthocyanidin as claimed in claim 28. Because claims 31-41 depend from claim 28, Hatano *et al.* does not anticipate claims 31-41. Applicant respectfully requests that the rejection be reconsidered and withdrawn.

Claim 55-56

Hatano *et al.* does not disclose a composition containing a therapeutically effective amount of a mixture of at least 70% pure proanthocyanidins as claimed in claims 55 and 56. As discussed above, the reference discloses an extract from Camellia japonica containing tannins. The reference does not disclose that the extract contains therapeutically effective amount of a mixture of at least 70% pure proanthocyanidins selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations thereof, and pharmaceutically acceptable salts of the foregoing proanthocyanidins.

Thus, the cited reference does not disclose, either literally or inherently, every element of the claimed compositon. Therefore, Hatano *et al.* does not anticipate a composition containing therapeutically effective amount of a mixture of at least 70% pure proanthocyanidins as claimed in claim 55. Because claim 56 depends from claim 55, Hatano *et al.* does not anticipate claim 56. Applicant respectfully requests that the rejection be reconsidered and withdrawn.

REJECTION OF CLAIMS 28-41 and 54-56 FOR OBVIOUSNESS-TYPE DOUBLE PATENTING

1) Rejection over U.S. Patent Application No. 09/748,748

Claims 28-41 and 54-56 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 14-15 of co-pending U.S. Patent Application No. 09/748,748. The Office Action alleges that the conflicting claims are not patentably distinct from each other because the co-pending application is allegedly directed to a drug product containing a composition for treating α-synuclein fibril formation containing a compound of Formula E which is epicatechin and a pharmaceutically acceptable excipient. The Office Action urges that the instant claims are directed to a pharmaceutical composition containing epicatechin and a pharmaceutically acceptable excipients in amounts within the co-pending application claims. The Office Action concludes that claims 28-41 and 54-56 are anticipated by claims 14-15 of the co-pending U.S. Patent Application No. 09/748,748. Applicant respectfully traverses the rejection.

Relevant Law

The disclosure of a patent cited in support of a double patenting rejection cannot be used as though it were prior art **even where the disclosure is found in the claims**. Obvious-type double patenting signifies that the difference between first-patented invention and its variant involves only an unpatentable difference, such that grant of the second patent would extend the right of exclusivity conferred by the first patent. Comparison can be made only with what **subject matter is claimed** in the earlier patent, paying careful attention to the rules of claim interpretation to determine what invention a claim defines and not looking to the claim for anything that happens to be mentioned in it as though it were a prior art reference. A fundamental rule of claim construction requires that what is claimed is what is defined by the claims taken as a whole, every claim limitation (each step) is material. *General Foods Corp. v. Studiengesellschaft Kohle mbH*, 23 USPQ 1839 (Fed. Cir. 1992).

Double-patenting has not been found in instances in which the claims at issue do not embrace the prior patent compounds and/or the claims in the prior patent do not suggest any modification that would have produced the claimed compounds in the patent or application at issue (see, *e.g., Ortho Pharmaceutical Corp v. Smith*, 22 USPQ2d 1119 (Fed. Cir. 1992)), in which obvious-type double patenting was not found in an instance in which the claims in the patent at suit were directed to compounds that did not encompass, structurally, the compounds claimed in the prior patents, and the compounds claimed in the prior patents did not suggest a modification of those compounds to produce compounds claimed in the patent at suit.

Thus, obvious-type patenting does not exist if the claims at issue do not encompass the claimed subject matter in the copending application, and, the claims in the copending application do not suggest a modification to produce the claims in the subject application.

Analysis

The pending claims would not extend the right of exclusivity of the claims of U.S. application Serial No. 09/748,748.

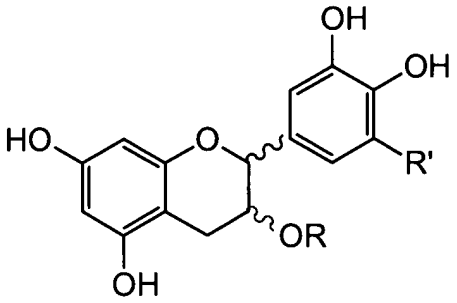
Claims of U.S. application Serial No. 09/748,748

Claims 14-15 of U.S. Application Serial No. 09/748,748, recite:

14. The method of Claim 1 where the compound is a compound of formula E or a pharmaceutically acceptable salt thereof.

15. The method of Claim 14 where the compound is selected from the group consisting of catechin, epicatechin, gallocatechin, epigallocatechin, and their gallate esters, and the pharmaceutically acceptable salts thereof.

Claim 1 discloses compounds of formula E as follows:

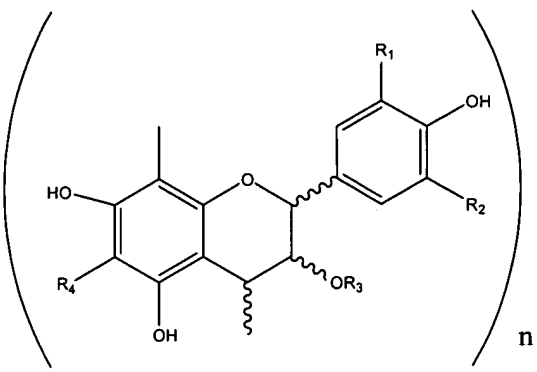


Formula E ,

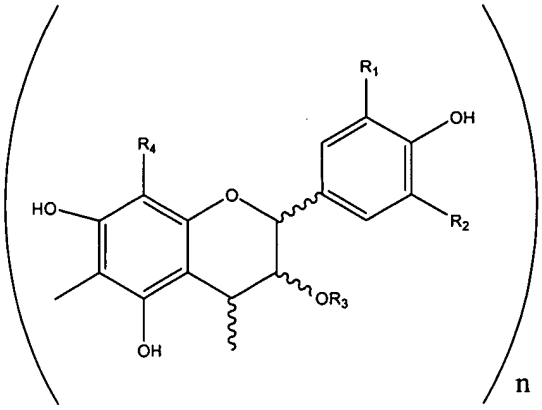
wherein the variables are as described therein.

Instant claims

Claims 28 and 55 are the independent claims in the instant application. As discussed above, instant claim 28 is directed to a pharmaceutical composition containing therapeutically effective amount of a proanthocyanidin, selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations of Formula I and Formula II, and pharmaceutically acceptable salts of the foregoing proanthocyanidins and a pharmaceutically acceptable carrier, diluent, or excipient, the therapeutic amount of the proanthocyanidin selected for efficacy in treating amyloid, α-synuclein or NAC fibrillogenesis in a mammalian subject. The claim describes formula I and II as:



Formula I



Formula II

wherein the variables are as described therein.

Claim 55 is directed to a pharmaceutical composition containing a therapeutically effective amount of a mixture of at least 70% pure proanthocyanidins, selected from a group of proanthocyanidins characterized by Formula I or Formula II, and proanthocyanidins characterized by oligomeric combinations of Formula I and Formula II. Dependent claims further define the proanthocyanidins in claimed compositions.

Applicant respectfully submits that claims 28-41 and 55-56, as amended herein, do not encompass compounds of formula E. Thus, the claims in the two applications are directed to different compounds. Therefore, the instantly pending claims would not extend the right of exclusivity of the claims of U.S. Patent Application No. 09/748,748. Reconsideration and removal of the rejection is requested.

2) **Rejection over U.S. Patent Application No. 10/053,625**

Claims 28-41 and 54-56 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 31-39 of the co-pending U.S. Patent Application No. 10/053,625. The Office Action alleges that the conflicting claims are not patentably distinct from each other because the co-pending application is allegedly drawn to a pharmaceutical composition containing or inherently containing the same compounds and a pharmaceutically acceptable excipient. The Office Action urges that the instant claims are directed to a pharmaceutical composition containing the same compounds and a pharmaceutically acceptable excipients of the application in amounts within the co-pending

application claims. The Office Action concludes that claims 28-41 and 54-56 are anticipated by claims 31-39 of the co-pending application No. 10/053,625. Applicant respectfully traverses the rejection.

Relevant law

As discussed above.

Claims in U.S. application Serial No. 10/053,625

Applicant notes that the Office Action cites claims 31-39 in U.S. application Serial No. 10/053,625 in support of the obviousness-type double-patenting rejection but the application only contains claims 1-38. Claims 31-38 of U.S. application Serial No. 10/053,625, recite:

> 31. A pharmaceutical agent comprising a therapeutically effective amount of a material made according to the process of claims 1, 8, 10-13, 18 or 22, the therapeutic amount of the material selected for efficacy in treating an amyloid disease in a patient.
>
> 32. A pharmaceutical agent comprising a therapeutically effective amount of a compound selected from the group consisting of chlorogenic acid and epicatechin, the compound and the therapeutic amount of the compound selected for efficacy in treating an amyloid disease in a patient.
>
> 33. The pharmaceutical agent of claim 31 or 32 wherein the therapeutically effective amount of a material comprises a dosage in the range of from about 10 to 1,000 mg/kg of body weight of the patient.
>
> 34. The pharmaceutical agent of claim 33 wherein the therapeutically effective amount of a material comprises a dosage in the range of from about 10 to 100 mg/kg of body weight of the patient.
>
> 35. The pharmacological agent of claim 33 wherein said amyloid disease for treatment is selected from the group of amyloid diseases associated with Alzheimer's disease, Down's syndrome, hereditary cerebral hemorrhage with amyloidosis of the Dutch type, the amyloidosis associated with type II diabetes, the amyloidosis associated with chronic inflammation, various forms of malignancy and Familial Mediterranean Fever, the amyloidosis associated with multiple myeloma and other B-cell dyscrasias, the amyloidosis associated with the prion diseases including Creutzfeldt-Jakob disease, Gerstmann-Straussler syndrome, kuru and animal scrapie, the amyloidosis associated with long-term hemodialysis and carpal tunnel syndrome, the amyloidosis associated with endocrine tumors such as medullary carcinoma of the thyroid, and the alpha-synuclein associated diseases including Parkinson's disease and Lewy body disease.

36. The pharmacological agent of claim 35 wherein said amyloid disease for treatment is Alzheimer's disease.

37. The pharmacological agent of claim 33 further comprising a pharmaceutically acceptable carrier, diluent, or excipient.

38. The pharmacological agent of claim 33 wherein the therapeutically effective amount of the material has an amyloid inhibitory activity or efficacy greater than 50%.

Claims 1, 8, 10, 13, 18 and 32 are directed to methods for isolating compounds that possess amyloid inhibitory activity from plant matter of the genus Uncaria. The claims do not disclose proanthocyanidins selected from proanthocyanidins of formula I or II or oligomeric combinations of formula I or II.

The Instant Claims

As discussed above.

Analysis

In an obviousness-type double-patenting analysis, the scope and content of the patent claim is determined relative to a claim in the application at issue; the differences between the two claims are determined; and the reasons why one of skill in the art would conclude that the claim in issue is an obvious variation of the cited patent claim that would extend the right of exclusivity of the cited patent claim are set forth (MPEP §804).

The pending claims would not extend the right of exclusivity of the claims of U.S. Patent Application No. 10/053,625.

The claims in U.S. Patent Application No. 10/053,625 recite a pharmaceutical agent that possesses amyloid inhibitory activity isolated from plant matter of the genus Uncaria; there is no recitation of proanthocyanidins of formula I or II nor of oligomeric combinations thereof. Accordingly, the compositions claimed in the instant applications are not obvious extension of the composition of U.S. Patent Application No. 10/053,625.

As noted above, double-patenting has not been found in instances in which the claims in the prior patent do not suggest any modification that would have produced the elements of the claims in the patent or application at issue (see, e.g., *Ortho Pharmaceutical Corp v. Smith*, 22

USPQ2d 1119 (Fed. Cir. 1992)). In this instance, the claims at issue recite therapeutically effective amount of specific compounds in a pharmaceutically acceptable carrier, diluent, or excipient. The claims of U.S. Patent Application No. 10/053,625 do not recite therapeutically effective amount of proanthocyanidins of formula I or II, oligomeric combinations thereof, or pharmaceutically acceptable salts thereof. Neither do the claims suggest any modification that would have led to compositions containing therapeutically effective amounts of specifically recited compounds of the instant compositions. Therefore, as between U.S. Patent Application No. 10/053,625, and the instant application, obviousness-type double patenting does not exist.

3) **Rejection over U.S. Patent No. 6,264,994**

Claims 28-41 and 54-56 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18 of U.S. Patent No. 6,264,994. The Office Action alleges that the conflicting claims are not patentably distinct from each other because the patent is allegedly drawn to a pharmaceutical composition containing or inherently containing the same compounds and a pharmaceutically acceptable excipient. The Office Action urges that the instant claims are directed to a pharmaceutical composition containing the same compounds and a pharmaceutically acceptable excipients of the patent in amounts within the co-pending application claims. The Office Action concludes that claims 28-41 and 54-56 are anticipated by claims 1-18 of U.S. Patent No. 6,264,994. Applicant respectfully traverses the rejection.

Relevant law

As discussed above.

Analysis

The pending claims would not extend the right of exclusivity of the claims of U.S. Patent No. 6,264,994

As discussed above, obviousness-type double-patenting is determined using the principles of claim interpretation. In an obviousness-type double-patenting analysis, the scope and content of a patent claim is determined relative to a claim in the application at issue; the differences between the two claims are determined; and the reasons why one of skill in the art

would conclude that the claim in issue is an obvious variation of the cited patent claim that would extend the right of exclusivity of the cited patent claim are set forth (MPEP §804).

As discussed below, it is respectfully submitted that that the instant pending claims would not extend the right of exclusivity of the claims of U.S. Patent No. 6,264,994.

Claims

Claims of U.S. Patent No. 6,264,994

The only independent claim of U.S. Patent No. 6,264,994 recites:

> A composition comprising plant matter from the plant commonly known as cat's claw, and plant matter from at least one plant selected from the group of plants consisting of, and commonly known as, ginkgo biloba, rosemary, gotu kola, and bacopin.

Dependent claims further define the composition and the plant matter in the composition.

Claims of the instant application

As discussed above.

Analysis

As noted above, a finding of obviousness-type double patenting requires an analysis of the claims based upon the principles of claim interpretation and do not use the claims of the prior patent as disclosure. The issue is whether granting of a patent on the second set of claims extends the right of exclusivity to the claimed compositions. The claims in U.S. Patent No. 6,264,994 recite a composition containing plant matter from the plant commonly known as cat's claw, and plant matter from at least one plant selected from the group of plants consisting of, and commonly known as, ginkgo biloba, rosemary, gotu kola, and bacopin; there is no recitation of proanthocyanidins of formula I or II nor of oligomeric combinations of formula I or II, nor of therapeutically effective amount thereof. Accordingly, the claimed compositions are not obvious extension of the composition of the patent.

As noted above, double-patenting has not been found in instances in which the claims at issue do not embrace the prior patent claims or the claims in the prior patent do not suggest any modification that would have produced the elements of the claims in the patent or application at issue (see, e.g., *Ortho Pharmaceutical Corp v. Smith*, 22 USPQ2d 1119 (Fed. Cir. 1992)). In this

instance, the claims at issue recite therapeutically effective amount of specific compounds in a pharmaceutically acceptable carrier, diluent, or excipient . The claims of U.S. Patent No. 6,264,994 do not recite therapeutically effective amount of proanthocyanidins of formula I or II, oligomeric combinations thereof, or pharmaceutically acceptable salts thereof. Neither do the claims suggest any modification that would have led to compositions containing therapeutically effective amounts of specifically recited compounds of the instant compositions. Therefore, as between U.S. Patent No. 6,264,994, and the instant application, obviousness-type double patenting does not exist.

In view of the amendments and remarks herein, reconsideration and allowance of the application are respectfully requested.

Applicant hereby petitions under 37 C.F.R. §1.136 for a three (3) month extension of time. A check for $475.00 is enclosed for the three-month extension fee. Please apply any charges not covered, or any credits, to Deposit Account 06-1050.

Respectfully submitted,

Date: 3/29/04

Dale L. Rieger
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